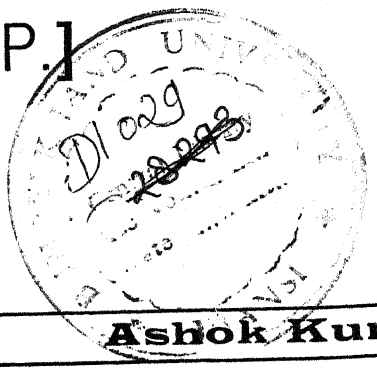
A CLINICAL AND IMMUNOLOGICAL STUDY OF BRONCHIAL ASTHMA IN CHILDREN

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(II)

C E R T I F I C A T E

This is to certify that the work entitled " A CLINICAL AND IMMUNOLOGICAL STUDY OF BRONCHIAL ASTHMA IN CHILDREN" has been conducted by ASHOK KUMAR under my direct guidance and supervision in the department of Paediatrics, M.L.B. Medical College, Hospital, Jhansi.

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Dated : 31st March 1993

Ashok Kumar

(ASHOK KUMAR)

I N D E X

Sl. No.	Particular	Page From	Page To
1.	INTRODUCTION ..	01	05
2.	REVIEW OF LITERATURE ..	06	38
3.	MATERIAL & METHODS ..	39	46
4.	OBSERVATIONS ..	47	67
5.	DISCUSSION ..	68	81
6.	SUMMARY & CONCLUSION ..	82	85
7.	BIBLIOGRAPHY ..	86	96
8.	APPENDIX ..	I	VII

INTRODUCTION

INTRODUCTION

Bronchial asthma is an episodic reversible inflammatory disorder of the obstructive airways disease, that is characterized by increased responsiveness of the tracheobronchial tree to a multiplicity of stimuli. Asthma is manifested physiologically by a wide spread narrowing of the air passages (Bronchospasm) increased bronchial mucus secretions and bronchial oedema. The patient presents with paroxysms of dyspnoea, chest tightness, cough and wheezing. In severe attacks there is tachycardia, pulsus paradoxus and central cyanosis. That is often reversible either spontaneously or with treatment. The air flow obstruction causes mismatching of alveolar ventilation and perfusion and increases the work of breathing. It is thought that varied etiology factors viz. biochemical, immunological, infective, endocrinal and psychological play and important role in causing an attack of asthma. These factors may or may not interact to produce classical symptomatology of the disease process.

The prevalence and incidence of asthma is observed that about 5-10 percent of children suffer from frequent wheezy episodes at some times in there childhood, the incidence increases to 20 percent if children having less

than 6 attacks of wheezing are included. Also, it has been observed that about half of the children presenting with asthma are atopic and show minor immuno-deficiencies (Sims et al 1981). Asthma could start at any age, although 80 to 90 percent of asthmatic patients have their first attack before the age of five years. Prior to puberty the sex incidence male : female is 2 : 1, thereafter, the sex incidence is equal (Ellis 1983).

Asthma may be extrinsic or atopic and intrinsic or nonatopic in nature. In extrinsic asthma, there is a strong family history of allergic diathesis in the family. High eosinophil count, abnormal CAMP metabolism and selective synthesis of IgE. Intrinsic asthma is often precipitated by infection specially by respiratory syncytial virus (RSV) or parainfluenza virus in infants and rhinovirus in patients who are more than two years of age. Recent studies show high IgE, atopic manifestation and eosinophilia in 10-30% cases of lower respiratory viral infections, indicating possible atopic component in these cases who subsequently develop asthma (Khatua et al 1987).

Asthma in children is usually, but not always of allergic type which occurs before 2 years of age and is precipitated by pollens, foods, house dust, mites, fungi and animal danger. It may be preceded by eczema. It is due mainly to type-I hypersensitivity reaction. Type-I hypersensitivity reaction is antigen antibody dependent. The reaction is initiated by allergen exposure, B cell stimulation and production of IgE. Then IgE binds with specific receptors, which are present on mast cell and basophil surfaces. On repeated challange by specific antigen the second stage of reaction comes into play with binding of antigen to the surface bound IgE.

The interaction between IgE and antigen provokes the release of mediators from granules inside the mast cells. This process known as degranulation, releases histamine, leukotrienes, eosinophil chemotactic factor of anaphylaxis (ECF-A) and prostaglandins that cause the symptoms of type-I hypersensitivity (Behrman and Vaughan 1990).

In some cases of asthmatic patients, there is another mechanism which play a role to produce type-I hypersensitivity like reaction. This involves IgG_4 (Sub-class of IgG).

Antibody mediating a complement form of type I reaction. According to Anderson (1984) non-immunologic mechanism also played a role in the pathogenesis of atopic disease named as anaphylactoid reaction (Non IgE mediated anaphylaxis like reaction).

In bronchial asthma, IgE level tends to be higher than normal (Johansson et al 1967, Berg 1969, Gleich 1970, Henderson 1971, Spitz 1972, Saha 1975, Lin 1977, Srivastava 1982, Hurbert 1982, Khatua 1987).

The term complement is applied to a system of factors occuring in normal serum that are activated characteristically by antigen antibody interaction and subsequently mediate a number of biologically significant consequences. Complement as it participates in immune-haemolysis comprises of components symbol C is used to denote complement components. In the order of their entry into reaction process, the complement components are designated i.e. C1, C2, C3, C4, C5, C6.. C9. In bronchial asthma some worker had shown decreased level of C3 and C4 (Halprin 1973; Kay 1974, Godfrey 1975, Delaney 1976, Arroyave-ure 1976, Hutcheroft 1978, Srivastava 1982). Other have shown its levels increased (Baur 1980, Srivastava 1982).

Among all the pulmonary function tests, spirometry, which records the volume of air into and out of lungs, is simple to measure. Measurement of the forced expiratory volume in 1 second (FEV), forced vital capacity (FVC) and peak expiratory flow rate (PEFR) provide a fairly reliable indicator of the degree of the airflow obstruction in case of bronchial asthma. Asthma severity can be judged by symptoms, medication requirements and objective measures of lung function.

Eosinophil leucocyte are significantly higher in bronchial asthma (Smith 1931, Lowell 1967, Orkankis 1970, Waklu 1974, Stickney 1974, Gupta 1975, Chazan 1976, CG Agarwal 2979, Arshod 1981, Lukza 1982, Acharya 1983). Parasitisation may alter the eosinophil count and IgE levels by their continuous antigenic stimulation of the immune system.

Keeping in view the above facts, a clinical and immunological study of bronchial asthma in children was undertaken to assess serum IgE, complement C3, C4, Absolute eosinophil count and spirometry.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Von Pirquet (1906) coined the word allergy to refer to a state of changed reactivity in a host "occuring as a result of contact with a foreign substance. He put together the Greek words "allos" meaning different or changed and "ergos" meaning work or action. This altered reactivity could either be beneficial to host as in the case of immunity or detrimental as in anaphylaxis.

Ellis (1983) defined allergic disorder as "adverse physiological reaction resulting from the interaction of antigen with humoral antibody and/or lymphoid cells". Bronchial asthma is one of the allergic disorders in which alteration in IgE, complement and eosinophils has been seen.

BRONCHIAL ASTHMA :

The term asthma is derived from the Greek word meaning "struggling for breath". There is no universally accepted definition of asthma. It may be regarded as a chronic inflammatory disorder of the airways in which many cells play a role, including mast cells and eosinophils.

Bruce (1958) observed that nearly 50 percent patients of asthma had a family history of allergy.

Vishwanath (1964) defined bronchial asthma as a syndrome that is characterised by attack of expiratory dyspnoea not attributable to disease of the heart or lung. The smooth muscle in the bronchi and bronchiols exhibit spasm, edema and exudation following exercise, natural exposure to strong odours, irritant fumes, tobacco, smoke, cold air, and intentional exposure to parasympathomimetic agents.

Ellis (1983) observed that eighty to ninety percent of asthmatic children had their first attack before the age of five years. Prior to puberty about twice as many boys as girls were affected. Thereafter, sex incidence was equal.

PATHOPHYSIOLOGY :

Whilst the bronchial hyper-reactivity results in bronchospasm with hypertrophy and hyperplasia of smooth muscles, the other essential ingredient of air flow limitation is an inflammatory reaction. In patients dying from asthma small airways are plugged with thick, viscid mucus, often forming casts. There is hyperplasia of goblet cells and basement membrane, sloughing of epithelium and submucosal infiltration with eosinophils, lymphocytes, mast cells and neutrophils (Warner 1984).

The obstruction produces increased airway resistance, which lowers the force of expiratory volume, and flow rates; causes premature closure of airways, hyperinflation of lungs; brings about increased work of breathing, change in elastic properties and frequency dependent behaviour of lung. Although airway obstruction is diffuse, it is typically nonuniform, from one part of the lung to another. This results in ill perfusion of inadequately ventilated portion of lung and leads to abnormalities of blood gases (Behrman and Vaughan 1987).

ETIOLOGY :

Asthma is a complex disorder involving biochemical autonomic, immunologic, infectious, endocrine and psychological factors. The control of the diameter of airways may be considered a balance of neural and humoral forces. Neural broncho-constrictor activity is mediated through the cholinergic portions of autonomic nervous system. Vagal sensory ending in airway epithelium, termed cough or irritant receptors, depending upon their location, initiate the afferent limb of reflex are which at the efferent end stimulate bronchial smooth muscle contraction. Humoral factor of broncho-dialation includes the endogenous

catecholamines which act on beta adrenergic receptors to produce relaxation in bronchial smooth muscles. In an individual patient a number of factors generally contribute, in varing degree, to the activity of asthmatic process (Behrman and Kliegman 1990).

CLINICAL MANIFESTATION :

Rackeman (1964) suggested seperating asthma into exterinsic atopic asthma caused by allergens or external factor and intrinsic or nonatopic asthma caused by non allergen factors.

Asthma presents with recurrent episodes of non-productive cough, chest tightness, dyspnea with prolonged expiration, tachypnea, wheezing, cyanosis, tachycardia and use of accessory muscles of respiration. Pain in abdomen may be present due to strenuous use of abdominal muscles and diaphragm. A barrel chest deformity is a sign of chronic, unremitting airway obstruction of severe asthma (Behrman and Kliegman 1990).

Warner et al (1992) classified asthma on the basis of severity and airflow obstruction as follow :

CLASSIFICATION OF ASTHMA ON THE BASIS OF SEVERITY AND AIR-FLOW OBSTRUCTION (WARNER ET AL 1992)

ASTHMA SEVERITY	CLINICAL FEATURES	LUNG FUNCTION	REGULAR MEDICATION USUALLY REQUIRED TO MAINTAIN CONTROL
Mild	.Intermittent, brief symptoms ⟨1-2 times a week.	.PEF ⟩80% predicted at baseline.	.Intermittent inhaled short acting $beta_2$ agonist (taken as needed) only.
	.Nocturnal asthma symptoms ⟨2 times a month.	.PEF variability ⟨20%	
	.A symptomatic between exacerbations	.PEF normal after broncho dilator	
Moderate	.Exacerbations ⟩1-2 times a week	.PEF 60-80% predicted at baseline.	.Daily inhaled anti-inflammatory agent.
	.Nocturnal asthma symptoms ⟩2 times a month.	.PEF variability 20-30%	.Possibly a daily long acting bronchodilator, especially for nocturnal symptoms.
	.Symptoms requiring inhaled $beta_2$ agonist almost daily.	.PEF normal after bronchodilator.	
Severe	.Frequent excerbations .Continuous symptoms .Frequent nocturnal asthma symptoms .Physical activities limited by asthma .Hospitalization for asthma in previous years. .Previous life threatening exacerbation.	.PEF⟨60% predicted at baseline. .PEF variability ⟩30%. .PEF below normal despite optimal therapy	.Daily inhaled anti-inflammatory agent at high doses. .Daily long acting bronchodilator especially for nocturnal symptoms. .Frequent use of systemic corticosteroids.

NOTE : . The characteristics noted in this table are general and the characteristics may overlap because asthma is highly variable. Furthermore, an individual's classification may change over time.

. One or more features may be present to be assigned a grade of severity.

ALLERGY IN ASTHMA :

Bruce Pearson (1958) elicitated that nearly 50% patients of asthma had family history of allergy.

Johnson (1967) found that 63% of patients with allergic asthma had raised IgE level in serum, while it was only 5% in those with non allergic asthma.

Robinson (1973) suggested that asthmatic paroxysm was triggered by the hypersensitivity reaction or by mental stress. Allergy was always a basic factor of an asthmatic paroxysm, as opined by the author.

Willium and Nicol (1973) observed that 90-95% of asthmatic children had atopic constitution to develop type - I hypersensitivity, demonstrated by skin pric testing to various allergens.

Gupta et al (1975) observed eosinophilia irrespective of the type of asthma, in their study.

Frick and Mills (1979) observed a role of viral infections in the allergic sensitization process. They studied 16 children including 2 cases, who had history of

atopy. Out of 16 children 11 developed clinical allergy and 5 developed asthma after an attack of respiratory viral infection.

Raihi et al (1990) showed an agreement existing between the history of asthma and allergy to house dust: bronchial challenge to whole house dust was positive. All allergic patients had significant bronchoconstriction, whereas, no reaction could be elicited in the non-allergic group.

IMMUNOLOGIC SYSTEM IN BRONCHIAL ASTHMA :

Immunologic system is the part of host defence, its primary function is to protect against invasion by infectious agent. Thes costs of this protection are allergy and auto-immunity. There are four major limbs of immune system : T lymphocyte, B lymphocyte, phagocyte and complement. Atleast twice the population of lymphocytes are involved in most of immune responses (Claman et al 1966 ,Devis et al 1967, Millar and Michel 1968).

Antigen induced asthma is representative of a type-Ihypersensitivity reaction. This specific response originates in the homocytotropic or reaginic antibody (immunoglobulins that can attack mast cells or basophils). But clinical significance is not clear in so called short term sensitizing antibody (Metcalfe et al 1981).

In 1982, Oshea observed that IgG may act like a reagenic antibody.

Anderson (1984) suggested that non-immunologic mechanism also played a role in the pathogenesis of atopic disease named anaphylactoid reaction (Non IgE mediated anaphylaxis like reaction).

Type-I hypersensitivity reaction is initiated by allergen exposure, B cell stimulation and production of IgE. IgE binds with specific receptors which are present on mast cell and bosophil surfaces. On repeated challange by specific antigen the second stage of reaction comes into play with binding of antigen to the surface bound IgE. When an antigen bridges atleast two IgE molecules, the cell is activated. The activated mast cells can then secrete mediatiors, that exist preformed in its granules. This process known as degranulation, releases histamine, leukotrienes, eosnophil chemotactic factor or anaphylaxis and prostaglandings that cause the symptoms of type-I hypersensitivity (Behrman and Vaughan 1987).

ROLE OF INFECTION IN BRONCHIAL ASTHMA :

The role played by infection in childhood asthma can only be estimated by empirical and indirect means. Even todate, no one seems to doubt that respiratory infection is the most important triggering factor in bronchial asthma. However, thorough investigation of 400 children referred from pediatrician under the diagnosis of pure infectious asthma showed that 373(95%) of them had other precipitating causes (Aask et al 1963).

Inflammatory reactions in the bronchi cause obstruction due to thickening of bronchial mucosa, increased secretion and impaired ciliary activity with long lasting undesirable changes in ventilation dynamics (Hall et al 1976).

Viral infection that produce airway epithelial damage, airway damage may expose the irritable airway receptators to react more easily to inhaled and other irritants (Empey et al 1976).

Respiratory infection may result in undesirable change in beta adrenergic tone and responsiveness to adrenergic stimulation (Busse et al 1977).

Infections with common bacterias and viruses do not influence the total serum IgE level. Serum IgE was reported to be elevated in an infant with para-influenza virus infection but did not appear to be an acute phase reactant (Sieber et al 1977).

There are several reasons why infection may precipitate bronchial asthma and particularly so in childhood, when the bronchial lumen is narrow. The mucosal lining becomes more readially swollen following infections than is the case in later life. In other words, infectious asthma may be considered an expression of the characteristic bronchial hyper activity to a number of different stimuli, rather than immunological hypersensitivity (Flahety 1977).

IgE IN BRONCHIAL ASTHMA :

In 1967, Ishizaka et al discovered that a reaginic skin sensitizing antibody belongs to a unique class of immunoglobulins which they called IgE.

Johansson et al (1970) found raised IgE level in bronchial asthma, atopic dermatitis and allergic rhinitis. He also noted that IgE level varied with age but not with sex.

Toda (1975) observed IgE level approximately 500,000 µg/kg of body weight and intravascular half life to be 2-3 days. The synthesis rate was 2.3 µg/kg/day. Thus, one third of the total body pool of IgE was replaced every day. Only 1% of the total IgE was cell bound.

Normal (1975) suggested that IgE was the principal mediator of immediate (type-I) hypersensitivity reactions.

Beavan (1976) reported that IgE binds to tissue mast cells and basophils. This cell bound complex then caused degranulation of basophils on combining with antigen (allergen) with the result that histamine and other mediators were released.

Homburger (1978)suggested that IgE concentration was generally raised in the allergic patients.

The IgE myeloma protein has a molecular weight of 1,90,000 with a sedimentation coefficient of 8s. It is a glycoproteins and like all immonoglobulins, it has a 4 chain structure, with two light and two heavy chains. The heavy chains like those of IgM, contain five domains which carry unique antigenic specifications, termed the epsilon determinants. It is those unique

antigenic structures which determine the class specificity of this protein. No other immunoglobulin heavy chain has epsilon antigenic determinants. The Fc fragment of immunoglobulin is responsible for the protein's ability to fuse to receptors on mast cells and basophils (Zeiss 1980).

GENETICS OF IgE :

The heritability of atopic disease was recognised as early as 1872. In most family studies a positive family history has been reported in 50-75% cases.

Adkinson (1920) proposed a recessive mechanism for inheritance of atopy but Spair and Cooke (1924), Bucher and Keeler (1930), favoured a simple Mandalian dominant inheritance.

Bray (1934) suggested a bimodal distribution of the onset of atopic disease.

Opree et al (1972) agreed with the observations that atopy was transmitted by two alleles at a single locus and that predisposition to atopy and synthesis of IgE were under identical genetic control.

Marsh (1974) analysed data from allergic families in terms of bimodal distribution and suggested recessive inheritance for high IgE levels.

Leung et al (1985) reported that T lymphocytes played an important role in the isotype specific regulations of the human IgE response.

DEVELOPMENT OF SERUM IgE LEVELS :

Johansson (1968) while reporting serum IgE levels in infants and children showed very low levels, compared to those of adults. Author found mean cord serum level of IgE to be 36 ng/ml (15% of adult). There was no correlation between the mean IgE level in the serum of newborns and their respective mothers. A gradual increase in the IgE level was found during childhood upto a mean level of 248 ng/ml in healthy adults, although the distribution was rather wide 61.4-1000 ng/ml (about 95% confidence limits), as the author wrote.

Berg et al (1969) reported serum IgE level in 132 healthy children who did not have any atopic disease. They also found a gradual increase in the mean IgE level from 137 ng/ml in the age group of 2-2½ years to 330 ng/ml in age group of 13-15 years.

In a longitudinal study of serum IgE level (Orgel et al 1975), 34 infants (from atopic and non atopic families) were followed for full one year. Neonatal levels ranged from 0-10 units/ml. The 50th percentile level increased from 2.2 units/ml at 2 weeks of age to

3.8 units/ml at 6 months of age and 9.8 units/ml at 9 months of age. Half of the cases in the study group, who maintained serum IgE level below 10 units/ml, included a high proportion of infants from atopic families. The basal serum IgE level of individual adults was relatively stable over periods of 0.5 to 5.5 years.

Ischizaka et al (1978) observed minimal concentration (0.25 ng/ml) of IgE antibody necessary to produce a positive Prausnitz-Kaustner (PK) reaction in man.

SERUM IgE LEVELS IN BRONCHIAL ASTHMA :

Johansson et al (1967 & 68) measured serum IgE levels by radio-immunosorbent assay (RISA) in 38 patients of asthmatic bronchitis after dividing them into allergic and non-allergic groups on the basis of skin and provocation test and on clinical grounds. Authors found significantly raised serum IgE level in 63% patients with allergic asthma. Compared to this only 5% of patients with non allergic asthma had raised level of IgE. IgE level of 700 ng/ml was taken as the arbitrary limit of normal value by the author. Mean concentration of IgE was six times higher in group with allergic asthma (1589 ng/ml) than in the group with non

allergic asthma (275 ng/ml); while mean level in the control group was 330 ng/ml. However, there was no significant difference in IgE levels, between the patient treated with steroids or hypo-sensitization and those not so treated. Moreover, there was no age difference in the IgE level as reported by the authors. Authors, further reported that no difference existed between allergic and non-allergic patients with respect to the concentrations of IgE, IgD, IgA and IgM in the serum.

Berg et al (1969) observed high serum IgE levels in 90 percent of the cases of perennial asthma and 50 percent cases of seasonal asthma. Patients with perennial asthma had markedly higher IgE concentration than those, whose asthma was essentially seasonal, probably owing to repeated or continuous exposure of children with perennial asthma to allergens. In contrast to the earlier studies, these authors found that IgE concentration increased after desensitization. Higher IgE concentration was found in patients with a positive response to allergy test and the concentration was twice as high during the pollination season, than before.

Gleich et al (1970) observed high serum IgE level in allergic asthma, and found higher IgE level in the group of untreated patients when compared to the group treated by hypo-sensitization. The finding suggested that IgE could decrease after hypo-sensitization (Johansson's 1969).

Henderson et al (1971) counted 76 percent of patients with higher IgE level, among allergic asthma cases as compared to only 21 percent, such patient among idiopathic asthma group, while taking 540 ng/ml as the arbitrary limit of normality. Workers explained that raised IgE levels in idiopathic group could be due to hidden allergic factors or other factors causing elevated IgE levels.

Spitz et al (1972) measured serum IgE with the use of Rowe modification of the mancini technique and showed significantly raised levels in atopic (357 ng/ml) and questionable atopic (233 ng/ml) patients when compared to normal person (88 ng/ml). Higher levels were also related to eosnophilia.

Loeffler et al (1973) reported high IgE levels with extrinsic asthma.

Key et al (1974) found that in 93 asthmatics patients (70 adults and 23 children) serum IgE levels was significantly higher.

Saha et al (1975) studied immunoglobulins IgG, IgD, IgA, IgM and IgE in the sera obtained from 69 bronchial asthma patients who were graded objectively according to atopic score. Among other associated atopic diseases, they often had allergic rhinitis. Nearly 91 percent of these patients had elevated serum IgE levels and mean level of serum IgE was more than 3.5 times higher than that observed in the normal subjects. Moreover, as their atopic score increased, serum IgE level also got elevated and every patient with high atopic score, had elevated serum IgE levels, indicating the association of atopic state with serum IgE level. Authors also reported a significant correlation between the intensity of intradermal test and prausnitz kustner (PK) reaction with serum IgE level.

Gupta et al (1975) observed increased IgE level in 39 percent patients of bronchial asthma. The detection of hyperimmunoglobulinaemia E in six out of twelve patient with peripheral eosinophilia and one out of five with normal counts suggests an association of eosinophilia counts with IgE level.

Lin et al (1977) found elevated serum IgE levels in 23 out of 35 asthmatic children and did not find any difference in mean serum IgE values among children presenting with normal or elevated IgM (347.1 IU/ml) values.

Kajosaari et al (1981) observed higher total serum IgE levels in atopic disease.

Srivastava et al (1982) found that serum IgE level was elevated above control level in all the three groups (age of onset, periodicity and duration of disease) of patients. However, within a perticular group no difference was noted in IgE level on the basis of duration and periodicity of disease. Level of IgE tended to be lower in patient with late onset asthma as compared to early onset asthma, but this difference was not statistically significant.

Herbert et al (1982) in their study of 72 cases found serum IgE value of over 150 KU per litre in 51 atopic asthma cases who showed positive skin test to 5 common allergens.

Tong et al (1986) found elevated total serum IgE levels in all 30 patients of extrinsic asthma. The range in age for all patients was from 4 to 13 years, with a mean of 8.2 years.

Khatua et al (1987) studied 59 random cases of bronchial asthma in children. Total serum IgE level measured by paper radio-immunosorbent test (PRIST) ranged from 25-580 KU/L except in cases with ascariasis who showed a range of 1410 - 2215 KU/L. Total serum IgE was higher in the higher age group of patients and in those who had a family history of allergy, more than 8 attacks in a year, positive radio-allergo-sorbent test and a sensitivity to larger number of allergens. The severity of the disease was not related to total or specific IgE.

THE CLINICAL RELEVANCE OF IgE :

Handerson (1971) showed that determination of serum IgE level did not help in any way, in the diagnosis and management of asthma and rhinitis. Similarly, loeffler (1973) demonstrated its uselessness in the diagnosis owing to wide variation observed in blood levels.

Orged (1975) demonstrated that elevation of serum IgE level at or before one year of age was highly correlated with atopic disease in the first two years of life. The elevation preceded the manifistations of atopy. Author concluded that IgE could be useful in

the prediction of allergy in small children with hereditary predisposistion. Kjellman (1976) also demonstrated a rise in serum IgE level, 6 months prior to the onset of allergic symptoms.

Use of serum IgE to differentiate atopic from nonatopic dermatitis, rhinitis and asthma has been questioned as O' Loughlin (1977) found raised level in many dermatoses and Nagaya (1979) proposed that there was no level of IgE, which could be used to rule out the presence of allergic disease.

Wang and patterson (1979) established the use of serum IgE measurement in the diagnosis and follow up of patients of bronchopulmonary aspergilosis (Nelson 1982).

Kajosaari and Searlnen (1981) showed that IgE could also help in the prediction of allergic disease among children with bronchiolitis, but single measurement of IgE was not useful.

Nelson (1982) examined the impact of the discovery of IgE on the clinical practice of allergy in 3 major areas.

(i) Use of measurements of total and specific IgE in the diagnosis of allergic disease.

(ii) To study the natural history of the development of allergic disease and study the impact of allergic immunotherapy.

(iii) To define significant allergens and cross allergenecity and to assess the quality of allergy extracts.

Bousquet et al (1984) discussed the predictive capacity of cord blood IgE in the development of allergy, in infancy and childhood. They opined that the risk of developing atopic disease (recurrent wheezy bronchitis and atopic dermatitis) was 5-10 times higher when the initial IgE was above + 1SD than when it was below this limit. Authors felt that the best predictive capacity was shown when both the family history of atopy and the titration of cord serum IgE were combined.

Johnw xynginger (1989), while quoting many authors explained that elevated levels of total serum IgE in bronchial asthma could help in the diagnosis. But, the author has cautioned that in other diseases also serum IgE level was raised viz - parasitic infestation, immunodeficiency, allergic rhinitis etc.

COMPLEMENT SYSTEM IN BRONCHIAL ASTHMA :

The name " complement " was initially chosen to describe the heat labile property of serum to complement the ability of antibodies to lyse red blood cells or bacteria. Today the name "complement" stands for a highly complex, maltimolecular, self-assembling biologic system that constitutes one of the major humoral mediators of inflammation.

The absence of deficiency of complement component has been recognized in persons with a wide varity of human diseases as well as in normal individuals. Complement deficiencies may be hereditary or acquired. Complement deficiencies are uncommon. However, some of the def iciencies are associated with characteristic clinical syndromes (Nusinow et al 1985).

Nomenclature of complement :

The term complement is applied to a system of factors, occurring in normal serum, which are activated characteristically by antigen-antibody intraction and subsequently mediat a number of biologically significant consequences. Study of the nature of complement has been concentrated to a large extent on the analysis of process of immune haemolysis and nomenclature proposed for

complement is based primarily on the haemolytic sequence. Complement, as it participates in immune haemolysis, comprises 9 components. It now appears established that these 9 factors are essentially similar, although not necessarily interchangeable, into species most studied (Austen et al 1968).

THE COMPONENTS OF COMPLEMENT :

A numerical notation is used for those complement components which participate directly in the reaction of immune haemolysis. Hitterto the numbers have been preceded by the symbol C'. It is now suggested that this usage be changed and that the symbol C be used to denote complement components.

In the order of their reaction the complement components should therefore, be designated C1, C2.... C9. The first component of human complement comprises 3 distinct protein sub components to which the provisional names C1q, C1r and C1s have been given. C1q was previously known as the 11s component or C'9 (Austen et al 1968).

The interaction between antigen and antibody can alter the configuration of a particular site in Fe region of the antibody molecule and make a receptor for the operation of first fraction (C1q) of first

component of the complement. Once the first fraction gets a place in the immune complex, following intraction between antigen and antibody, it acquires the ability to activate the rest of the complement components one after another in a sequence C1, 4, 2, 3, 5, 6, 7, 8 and 9 till a puncture or functional hole in the cell membrane is made and lysis of the cell occurs (Das Gupta 1976).

There are two main pathways of complement activation classical and alternate or properdin. In classical pathway the interaction starts at C1 level and finishes at C9 until cell lysis occurs and Fe portion of immunoglobulin is involved. Whereas, in alternate pathway the reaction start at C3 and is independent of Fe region and is usually poorly lytic. Once C3 is activated the remainder of components are activated in a standard cascade. The end point is lysis of the target cell by a complex consisting of C5b, 6, 7, 8, 9. The classic pathway may be activated by antigen antibody complexes and nonimmunologically by C reactive protein and trypsin like enzymes (Behrman and Vaughan 1989).

SERUM COMPLEMENT C3, C4 LEVELS IN BRONCHIAL ASTHMA :

Halprin et al (1973) observed decreased arteriovenous levels of complement in occupational asthma after bronchial challenge with fungal antigens.

Kay et al (1974) observed in their study that there was no significant difference between the circulating levels of C3 and C3 proactivator when adult and child asthmatics were compared with their respective normal controls. Moreover, the adult asthmatic patients had a higher total haemolytic component level (CH_{50}) than adult controls. But, differences between child asthmatics and the control subjects were not significant. These workers also found that a raised C4 level was associated with the features of allergic disease whereas, those with non allergic disease had low C4 level.

Codfrey et al (1975) reported that estimation of C4 levels did not prove useful in the classification of asthma since a normal C4 level were found in asthma patients.

Delancy et al (1976) observed normal C3, C4 complement and total haemolytic component levels in sixteen asthmatic patients with aspirin idiosyncrasy.

Arroyave et al (1976) detected the presence of activated C3 and factor B components by counter immunoelectrophoresis in the serum of asthmatic patients, who were challenged with skin test positive antigen, thus proving the activation of alternative pathway of complement system.

Weemass et al (1977) estimated significantly depressed C4 and C3 proactivator levels in child asthmatic patients as compared with controls.

Hutchcroft et al (1978) also found normal complement component levels (C3, C4, CH_{50}) in seven allergen induced asthmatic patients with no evidence of complement activation.

Steven et al (1979) observed a significant decrease in CH_{50} and non-significant decrease in C3 levels in eight patients, who showed positive bronchial reaction to allergen challenge.

Baur et al (1980) estimated significantly increased complement component levels (C3 and C4). Moreover, increase in CH_{50} level was seen in five out of sixteen asthmatic patients, during an immediate asthmatic reaction. The levels were also raised in seven patients during late asthmatic reactions.

Srivastava et al (1982) estimated complement component levels (CH_{50}, C4 and C3 proactivator) in one hundred thirty patients with bronchial asthma and fifty five healthy subjects. In sixtytwo patients the onset of the disease was before the age of 20 years. In sixty seven patients the asthmatic symptoms were of less than 5 years duration. Positive skin tests and family history of atopy were frequently seen in patients with early onset asthma. They observed a significantly decreased C3 level in patients suffering from perennial asthma and in those cases, who had a longer history of the disease. They did not observe any change in C3 proactivator and CH_{50} levels in asthmatic patients. Further, they found a significantly raised C4 level in patients with late onset asthma as compared to those with a history of early onset asthma.

Stevan et al (1985) found increased levels of complement component (C3, C4) in asthmatic patients.

EOSINOPHIL COUNT IN BRONCHIAL ASTHMA :

Eosinophil luckocyte are characterised by large coarse granules of prominent red colour seen after staining with Romanwasky stain and having a neucleolus with

single or two segments. They normally accounts for fewer than 5% of circulating lukocytes. Eosinophil count may be depressed by high levels of Adreno Cortical harmone and increased in parasitic and allergic disorders. Eosinophil count more than 5% in paripheral blood smear or 250 cells/mm^3 is considered elevated. Blood eosinophil in the allergic disorder does not exceed 15-20% but may occasionally be as high as 35%.

In asthma eosinophilia plays a dual part : protecting the patient from the effects of mast cell vasoactive mediators and simultaneously damaging the bronchial mucosa. Eosinophil neutralizes the slow realising substance (SRS) of anaphylaxis and histamine by enzymatic action and by phagocytosis. In course of neutralization of slow realising substance (SRS) of anaphylaxis eosinophil may undergo degranulation or autolysis, causing the release of major basic proteins. These major basic proteins damage the respiratory mucosa in concentration as low as 10 ug/litre (Wasserman et al 1975).

Bray GW (1931) and Smith (1931) found that eosinophilia is predominantly associated with allergic disorders.

Lowell (1967) reported that measurement of total eosinophil count in circulating blood was helpful in the evaluation of asthmatic disease. In his study 28 patients and elevated eosinophil count ($7350/mm^3$). He also noticed that eosinophilia was lacking in patients of bronchial asthma as a result of intercurrent infections or because of eosinophil supression by bronchodilator drugs.

Orkankis et al (1970) found eosinophilia in 85% patients of bronchial asthma.

Sharma et al (1974) observed elevated eosinophil count in 71.8% patients of bronchial asthma.

Gupta et al (1975) observed eosinophilia, irrespective of the type of asthma in their study.

Shahi et al (1976) found that in 24 patients of bronchial asthma total eosinophil count was significantly higher (441 ± 384/cmm) than in control cases (119 ± 88/cmm). But no correlation was observed between the eosinophil count and T or B lymphocyte counts.

Agarwal et al (1979) in his study found that patients with bronchial asthma had significantly high absolute eosinophil count 917.71 ± 618.9 compared to control cases (231.4 ± 105.4/cmm). A direct correlation

was observed between absolute eosinophil count and T cells percentage.

Arshod (1981) observed eosinophilia in bronchial asthma.

In 1982, Lukza et al in his study found that acute asthma was associated with eosinopenia while chronic and stable asthma showed eosinophilia. The detail of observations are as follows :

Type of asthma	Absolute eosinophil count	Mean
Acute asthma	170 x 10^9 litre	21 x 10^9 litre
Chronic	2340 x 10^9 litre	1048 x 10^9 litre
Stable	1950 x 10^9 litre	345 x 10^9 litre

Acharya et al (1983) carried out their study in childhood asthma. They studied 300 cases of childhood asthma, diagnosed clinically and found eosinophilia in 45.3% of the cases which were having absolute eosinophil count 7400 cells/mm^3 while 710% eosinophilia was found in 23% cases and 740% eosinophilia was observed in 5 out of 300 cases.

SPIROMETRY IN BRONCHIAL ASTHMA :

Pulmonary function studies are essential for diagnosing and assessing the severity of asthma in patients. Objectives measurements of lung function for monitoring asthma are analogous to measurements in other chronic disease situations, for example measuring blood pressure with a sphygmomanometer for hypertension (Kjellman et al 1992).

Estimation of ventilatory capacity helps in the treatment of bronchial disease. Some diseases cause narrowing of the airway during expiration such as asthma and chronic bronchitis. The forced expiratory volume (FEV), forced vital capacity (FVC) percentage are reduced some times to 40% or less. This is due to a greater reduction in FEV than FVC (Davidson 1986).

FVC (forced vital capacity) is the largest volume of air measured on complete expiration after the deepest inspiration, and that expiration being as forceful and rapid as possible. This volume is significantly reduced in chronic restrictive pulmonary disease due to air trapping (Guyton 1991).

FEV_1 (Forced expiratory volume) is usually calculated in one second. This tests the volume of air exhaled over a given time period, during the performance of a forced expiration. If it is below the predicted normal volume, then this gives a information regarding the severity of the expiratory air way restriction.

FEF (forced expiratory flow) formerly called MEFR (maximum expiratory flow rate). This is the average rate of flow for a specified portion of the forced expiratory flow, usually calculated between 200 ml and 1200 ml on the chart. A slowed rate is an early sign of chronic obstructive pulmonary disease. Patient is normal if his one second rate is not below 70 percent. If it is below 70 percent, he is likely to have some obstructive disease such as bronchial asthma, chronic bronchitis or pulmonary emphysema. If one second volume observed after the administration of a bronchodilator, shows an improvement of 20% or more the patient probably has bronchial asthma which is distinct from pulmonary emphysema (Guyton 1991).

In case of obstructive disease such as pulmonary emphysema or bronchial asthma, the bronchiolar collapse occur during forced expiration. This is called as "check value" effect.

When treating asthmatic patients, it is often desirable to make frequent objective assessments of PEF, usually more than once a day. Daily or circadian variation in PEF reflects the severity of asthma (Kjellman et al,1992).

In case of bronchial asthma the FEV/FVC percentage is greatly reduced, sometimes 20% or less in reference to normal control, which is between 68-80% (Guyton 1991).

Pulmonary function testing is valuable in the evaluation of children in whom asthma is suspected. In those known to have asthma, such tests are useful in assessing the degree of airway obstruction (Behrman and Vaughan 1987).

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MATERIAL & METHODS

MATERIAL & METHODS

The present study was conducted at the Allergy Clinic, Immunology and Biochemistry laboratory, Department of Paediatrics, M.L.B. Medical College and Hospital, Jhansi. A total number of 21 children between 4 and 13 years of age attending the Paediatrics Out Patient department and Allergy Clinic were selected for this study. Cases were grouped as follows :

A - Study group :

Sixteen children of bronchial asthma were selected from the out patient department and Allergy clinic of Paediatrics department, M.L.B. Medical College, Jhansi. Those childfen having liver disorder, renal disorder known immuno-deficiency disease and receiving corticosteroid were excluded from the study. Diagnosis were based on detailed history, clinical examination and relevant investigations.

B - Normal healthy controls :

Five children those of the staff members of the hospital with no history of allergic disorder, no history of atopy in family, no intestinal parasitic infestation were taken as control cases for this study.

Present, Past and Family history :

From parents or other family members detailed history was obtained regarding present illness, in a chronological order. Beside name, age, sex, address and socio-economic status, following facts were recorded in each case : a detailed history with emphasis on the age at the onset of the first attack; duration of disease; symptom free period; frequency per year; precipitating factors for illness.

The other detail recorded was that of history regarding environmental exposure to allergens. An attempt was made to elicit the role of food, drugs and physical agents in initiating or aggrevating the symptoms of asthma.

Past History :

History of worm infestation, bronchiolitis pertussis and measles was elicited.

Family History :

History of atopy especially that of bronchial asthma in other family members, tuberculosis in any family member was elicited.

Immunization history :

History of immunization was asked from the parents. For BCG vaccination, confirmation was done from the scar mark.

Social history :

A detailed account of living conditions of the patients was noted, with special reference to the type of house (Kaccha/Pacca), flooring, water supply and toilet facilities. The status of hygiene was noted, as well.

Physical examination :

Besides routine physical examination of the whole body, a record of the detailed examination of the system(s) involved was made. Thorough clinical examination was done especially to note wheezing, nasal/congestion and rhinorrhoea.

Central nervous system, cardiovascular system and respiratory system were examined in each cases. Main emphasis was given to respiratory system. Lung capacity was measured by spirometry in each cases. Abdomen was specifically examined for liver, spleen enlargement and tenderness of colon.

Children with bronchial asthma were assessed on the basis of their personal history of allergy, family history of allergy, degree of eosinophilia, decrease in lung capacity and age of onset of illness.

Weight :

Weight was recorded nearest to 0.05 kg by using infant weighing scale, if the weight was less than 10 kg. Adult type weighing machine was used in children weighing more than 10 kg and weight was recorded nearest to 0.1 kg.

Investigations :

The following investigation were done in each case :

1). Total and differential leucocyte count.

2). Haemoglobin.

3). Erythrocyte sedimentation rate (ESR).

4). Stool examination for ova and cysts.

5). Chest skiagram.

6). Estimation of IgE level in serum.

7). Estimation of C3, C4 level in serum.

8). Absolute eosinophil count (AEC)
AEC = TLC x Percentage of eosinophil/100.

9). Peak expiratory flow (litre/minutes) by Peak flow meter.

Collection of blood sample :

From each patient blood sample of 6 ml was collected by a sterile dry syringe from the anticubital vein. Total leucocyte count was done by neubaur chamber and differential count was done after making a smear and staining with Leishman stain. Erythrocyte sedimentation rate was done. Absolute eosinophil count was calculated with the help of following formula.

$$\text{Absolute eosinophil count} = \frac{\text{Total leucocyte count} \times \% \text{ of eosinophils}}{100}$$

The serum was separated within 30 minuts after collection of sample and was kept in a freezer at-20°C.

IgE estimation :

Serum level of IgE was measured by single radial immuno-diffusion technique (Mancini 1965) using low concentration commercially prepared IgE plates and IgE standard serum. Automatic micro pipettes were used to make different dilutions of the standard serum and for filling the wells.

20µl of the serum (standard or patient serum) was placed into the wells, followed 30 minutes later, by another 20 µl : thus, making total volume of 40 µl per well for the quantitative determination of IgE.

After loading, the plates were allowed to stand open for 10 minutes and then close with the plastic lid,the plates were subsequently left standing at room temperature.

The diameter of precipitin rings was read off with an accuracy of 0.1 mm after allowing diffusion to occur for five days.

Reference curve was drawn after plotting the square of diameter on x-axis against the known concentration (IU/ml) of reference serum plotted on Y-axis.

The concentration of the IgE in the sample was then read off directly on this straight line.

This method of IgE estimation was sensitive to detect serum IgE level between 920 Iu/ml and 11.000 Iu/ml.

Complement C3 and C4 estimation :

Serum level of complement C3, C4 were measured by single radial immuno-diffusion technique (Mancini 1965) using commercially prepared low concentration C3, C4 plates and C3, C4 standard serum 5 µl capillary tubes were used for filling the wells. Automatic micro pipettes were used to make different dilutions of the standard serum.

5 µl of serum (standard or patient serum) was placed into wells, for quantitative determination of complement C3 & C4.

After loading, the plates were allowed to stand open for 10 minute, than closed with the plastic lid and left for the development of the precipitin rings in inverted position at room temperature.

The diameter of precipitin rings was read off at an accuracy of 0.1 mm after diffusion was allowed to take place for three days.

Reference curve was drawn after plotting the square of diameter on x-axis against the known concentration (mg/ml) of reference serum plotted on Y-axis.

The concentration of the complement C3 and C4 in the sample was then read off directly on this straight line.

Measurement of lung capacity by peak flow meter :

Lung capacity was measured by peak flow meter in each case on each visit and on every day in admitted cases.

Forced expiratory volume by peak flow meter :
(Litre/Minute)

The patient was asked to take in deep breath as for as possible and then expel the same as hard and as fast as possible into the peak flow meter. Reading was noted from the indicator of peak flow meter.

OBSERVATIONS

OBSERVATIONS

A prospective study was carried to assess serum immunoglobulin E, serum complements, peak expiratory flow (litre/minutes) by peak flow meter and absolute eosinophil count in bronchial asthma of children. The present study was conducted in the out patient department of Paediatrics, Allergic Clinic of department of Paediatrics and Immunology and Biochemistry laboratory of the Paediatrics department, M.L.B. Medical College & Hospital, Jhansi, during the period of 16 months from November 1991 to February 1993.

The present study comprised of 21 children of 4 years to 13 years age. Out of these, 16 children were suffering from bronchial asthma. Five healthy cases of comparable age groups who had no present, past and family history of allergy or bronchial asthma, served as a control group in this study. Control cases were selected from among the children of hospital staff.

A detailed history was taken and thorough clinical examination was done in each case. Microscopic examination of stool was performed to detect parasitic ova and cysts. Haemoglobin, total leucocyte count, differential

leucocyte count and erythrocyte sedimentation rate were done and absolute eosinophil was calculated in all the cases. Spirometry, serum complement components C3, C4 and immunoglobulin E were estimated in all the cases.

TABLE - I : Frequency distribution of cases into different study groups

Clinical groups	Number		Cases with positive family history of Bronchial asthma.
Bronchial Asthma-			16
Seasonal	13	16	
Perennial	03		
Control	05		Nil
Total	21		16

1. The study group :

The study group comprised of 16 patients of bronchial asthma with seasonal and perennial symptoms. Thirteen cases had seasonal symptoms and 3 cases had perennial symptoms. Family history of bronchial asthma was positive in all cases.

TABLE - II : Showing the distribution of patients according to age and sex.

Age groups (yrs)	Number of cases		Total
	Male	Female	
0 - 3	Nil	Nil	-
4 - 6	03	-	03
7 - 9	03	03	06
10 - 12	05	01	06
13 - 15	01	-	01
Total	12	04	16

2. Age and sex distribution :

Table II show that all 16 patients of bronchial asthma, were below 13 years of age. Maximum number of cases were in 4 to 12 years age group. Youngest case was 4 years old and oldest case was 13 years old.

Sex distribution showed that 12 patients were males and 4 were females, out of 16 cases.

TABLE - III : Showing the general characteristics of cases.

Characteristics	Study group	Control group
1. Occupation :		
Students	14	5
Miscellaneous	02	0
2. Residence :		
Pucca	15	5
Kaccha	01	0
3. Home set-up :		
Rural	03	0
Urban	13	5
4. Dietary habits :		
Vegetarian	06	3
Non-vegetarian	10	2
5. Methods of excretadisposal:		
Flush type	13	5
Field system	02	0
Daily system	01	0

3. General characteristics of cases :

Table III shows that subjects belonged to various categories and had different general characteristics.

Among 16 cases, 14 were students and two was illitrate. Majority of cases were having their pucca houses. Only one case had kaccha house.

TABLE - IV : Showing the number of cases according to age at onset of symptoms of disease.

Age group (yrs)	Number of cases	
	Male	Female
∠ 1 yrs	1	0
1 - 3	5	0
4 - 6	3	4
7 - 9	3	0

4. Onset of symptoms :

Table IV shows the number of cases according to age at onset of symptoms of bronchial asthma in both sex.

All the 16 cases had onset of wheezing or breathlessness before 9 years of age. Majority of male children had onset of symptom between 1 to 6 yrs of age. All 4 females had onset of symptoms between 4-6 years of age.

TABLE - V : Showing distribution of cases according to duration and periodicity of asthma in study group sex wise.

Sex	Duration of asthma Number of cases		Periodicity Number of cases	
	⟨5 yrs	⟩5 yrs	Seasonal	Perennial
Male	08	04	09	03
Female	03	01	04	-
TOTAL	11	05	13	03

5. Number of cases according to duration and periodicity :

Table show the distribution of number of cases according to duration of bronchial asthma. Out of 16 cases of bronchial asthma 11 cases (8 male & 3 female) were had less than 5 years of duration, and 5 cases (4 male & 1 female) had more than 5 years duration of asthma.

Thirteen cases (9 male & 4 female) had seasonal (less than 6 attack peryear) and 3 (male) cases had perennial (symptom persisting throughout the year) symptom.

TABLE - VI : Showing Hb%, blood counts, ESR in study group and control group

Group	Sex	No.of cases	Hb(gm%) mean (range)	TLC (per cmm) Mean (range)	Differential leukocyte count (%) P mean (range)	L mean (range)	E mean (range)	M mean (range)	ESR(wintrobe) mm in Ist hour mean (range)
(A) Bronchial asthma	M	12	11.6 (9.2-14.0)	7931 (6700-11080)	46.9 (36-63)	40.5 (32-60)	6.2 (2-18)	-	30 mm (6-56)
	F	04	9.7 (9.2-105)	8700 (6100-9800)	52 (45-60)	31.5 (30-44)	8.5 (3-11)	-	19.5 (16.30)
	B	16	11.1 (9.2-14.0)	10823 (6100-11080)	48.1 (36-63)	35.3 (30-60)	7.0 (2-11)	- -	27.3 (5-56)
(B) Control	M	03	13.8 (13.5-14.0)	8100 (7600-8700)	50.6 (46-54)	34.6 (46.52)	2 (1-3)	1 (0-2)	15 (11-18)
	F	02	13.2 (13.0-13.5)	7850 (7200-8500)	50.0 (48-52)	47.0 (46-48)	0	2 (0-3)	13 (13-15)
	B	05	13.6 (13.0-14)	8000 (7200-8700)	50.4 (56-54)	40.0 (46-52)	2 (1-3)	1.4 (0-3)	14 (11-18)

P = Polymorph, L = Lymphocyte, E = Eosinophil, M = Monocyte,
Hb= Haemoglobin,
M = male, F = Female, B = Both.

6. Haemoglobin level, blood count, ESR in the study and control group :

Cases of bronchial asthma showed higher mean eosinophil count (7%) and higher mean ESR (27.3 mm in Ist hour) as compared to control cases (E-2% and ESR 14.2 mm in Ist hour).

In the same way there was not much difference in eosinophil counts between male and female bronchial asthma cases.

Haemoglobin percentage in bronchial asthma patients was less than that observed in control cases. Leukocyte counts did not show much difference between asthmatic and healthy control group of cases.

TABLE - VII : Absolute eosinophil count in study group and control group.

Group	Sex	No.of Cases	Mean & range	Duration of Bronchial asthma		No. of cases having eosinophilia	
				≤5 yrs (Mean & range)	>5 yrs (mean.range)	≥250/mm^3	≥500/mm^3
Study group	M	12	397 (89-1008)	-	-	7	3
	F	04	644 (584-736)	-	-	0	4
	B	16	459 (89-1008)	263/mm^3 (89-730)	535/mm^3 (312-1008)	7	7
Control group	M	03	25.3 (00-76)	-	-	0	0
	F	02	0	-	-	0	0
	B	05	15.2 (00-76)	-	-	0	0

7. Absolute eosinophil couht in the study group and control group :

Table VII shows absolute eosinophil count in the study group and control group of cases. Table VII also shows variation of eosinophil counts with respect to sex and duration of disease. Mean absolute eosinophil count was ⁄250/cmm in control group, whereas, it was more than 250/cmm in the study group.

Seven out of 16 cases of bronchial asthma had absolute eosinophil count more than 250/cmm, while no control case had eosinophil count of more than 250/cmm. Other 7 cases had absolute eosinophil count of more than 500/cmm, of which 3 were males and 4 females. Mean absolute eosinophil count was less (263/cmm) in those cases who had asthma of less than 5 years duration as compared 535/cmm in those who had asthma of more than 5 years duration.

TABLE - VIII : Serum complement levels in study group and control group according to sex.

Test Serum complement	Study group				Control group			
	Sex	No.of cases	Mean	Range	Sex	No.of cases	Mean	Range
(1) C3 mg/ml	M	12	0.95	(0.86-1.1)	M	03	1.14	(1.15-1.20)
	F	04	1.04	(0.99-1.15)	F	02	1.21	(1.2-1.22)
	B	16	0.97	(0.86-1.15)	B	05	1.19	(1.15-1.22)
(2) C4 mg/ml	M	12	0.28	(0.24-0.33)	M	03	0.27	(0.26-0.30)
	F	04	0.29	(0.24-032)	F	02	0.30	(0.28-0.32)
	B	16	0.28	(0.24-0.33)	B	05	0.28	(0.26-0.32)

M = Male, F = Female, B = Both.

8. Serum complement C3 and C4 levels in bronchial asthma in children according to sex.

In all, cases of bronchial asthma, included in our study had family history of atopy. Serum complement level in bronchial asthma is shown in table no. VIII.

Complement C3 :

Mean serum C3 level (0.97 mg/ml) in bronchial asthma was lower than that observed in control cases (1.19 mg/ml). This difference was more marked in male asthmatic cases, whose mean C3 level (0.95 mg/ml) was lower as compared to male control cases (1.14 mg/ml). The difference in female asthmatic cases and female control cases was not marked (1.04 mg/ml and 1.21 mg/ml respectively).

Complement C4 :

Pooled mean C4 level was similar in the study group (0.28 mg/ml) and control group (0.28 mg/ml) of cases. In the same way there was no apparent difference in C4 levels of male and female cases when compared to their respective controls.

TABLE - IX : Serum complement C3 and C4 levels in study group and control group according to duration of disease and periodicity.

Serum test (Complement)	Study group: Duration of disease (Bronchial asthma)		Periodicity		Control group
	< 5 years (Mean and range)	> 5 years (mean and range)	Seasonal (Mean & range)	Perennial (Mean & range)	(Mean and range)
C3 mg/ml	0.98 (0.86-1.15) n = 11	0.95 (0.88-1.1) n = 5	0.97 (0.86-1.15) n = 13	0.95 (0.86-1.1) n = 3	1.19 (1.15 to 1.22) n = 5
C4 mg/ml	0.28 (0.24-0.33) n = 11	0.29 (0.28-0.34) n = 5	0.28 (0.24-0.33) n = 13	0.27 (0.28-0.32) n= 3	0.28 (0.26-0.32) n = 5

n = number of cases.

9. Serum complement C3 and C4 level in study and control group according to duration of asthma and periodicity :

Patients were divided into two groups depending upon duration of bronchial asthma, (less than or more than 5years duration) and periodicity (Episode : less than 6 attack per year, perennial : symptom, persisting throughout the year). History of atopy, i.e. family history of allergy, was present in all the cases of study group.

In eleven patients asthmatic symptoms were less than 5 years of duration, and in 5 patients symptoms were more than 5 years of duration. Out of sixteen patients only three patient had perennial asthma.

Serum complement level in bronchial asthma is show in table no. IX.

Complement C3 :

Mean serum C3 level was almost the same in patients with perennial asthma and those who had seasonal asthma (0.95 mg/ml and 0.97 mg/ml) respectively; both values were appreciably lower than that observed in control group (1.19 mg/ml). Complement C3 level was also the same in patients with asthma of more than 5 years duration and those whose asthma was of less than 5 years duration

(0.95 mg/ml and 0.98 mg/ml) respectively. Mean complement C3 level in control group was 1.19 mg/ml.

Complement C4 :

No difference in the level of C4 was observed between the asthmatic and non-asthmatic cases. Moreover, duration and periodicity of asthma did not make any difference to complement C4 level.

TABLE - X : Serum IgE level in study group and control group according to age.

Clinical group	Age (years)	Serum IgE (IU/ml) (range)	No.of cases	Comments
1) Study group	4-06	⟨920 - 2870	3	One case had ⟨920 IU/ml and 2cases had 2550 & 2870 IU/ml
	7-09	⟨920-2760	6	4 cases had ⟨920 IU/ml and 2 cases had 2680 & 2760 IU/ml.
	10-12	⟨920-3860	6	3 cases had ⟨920 IU/ml and 3 cases had (2850-3860).
	13-15	2580	1	
2) Control group	5-13	⟨ 920	5	All control group cases had IgE ⟨ 920 IU/ml.

10. Serum IgE level in the study group and control Group according to age :

Serum IgE levels was measured in 5 healthy children and 16 children of bronchial asthma with a history of atopy present in all cases. Table X show serum IgE level in various age groups.

Out of 16 cases of bronchial asthma eight cases had IgE level more than 920 IU/ml and all control cases had serum IgE level less than 920 IU/ml.

Serum IgE level did not vary significantly, with age.

TABLE - XI : Serum IgE level in study group and control group according to duration of asthma and periodicity.

Serum	Study group				Control group
	⩽ 5 yrs (Duration of disease)	> 5 yrs	Seasonal	Perenn-ial	
IgE IU/ml	⩽920-2860 n = 11	⩽920-2890 n = 5	⩽920-3860 n = 13	2850-2890 n = 3	⩽920 IU/ml n = 5

n = number of cases.

11. Serum IgE level in study group and control group according to duration of disease and periodicity :

Table XI show that all three cases of perennial asthma had raised IgE level (7920 IU/ml) but in seasonal asthma only five patients (38%) had raised IgE 7920 IU/ml, rest of eight patient had serum IgE level ⟨920 IU/ml (61%). However, no difference was noted in IgE level on the basis of duration of asthma.

Analysis of Bronchial asthma patient with serum IgE level 7 920 IU/ml :

Table XII show 8 cases in the present study had high IgE level. In these cases age ranged from 4 years to 13 years and the duration of disease was 1½ yrs to 9 yrs. Absolute eosinophil count ranged from 156 to 728/cmm. All the 8 cases had positive history of atopy. None of the cases had parasitic infection. Analysis of these cases revealed that higher IgE values in the present study was not invariably associated with eosinophilia or history of atopy.

TABLE - XII : Analysis of Bronchial asthma patient with serum IgE level 7920 IU/ml.

Sl. No.	Patient Age/Sex	Duration of disease	Intestinal parasitic infection	Family/ history of atopy	Leucocyte count (Per Cmm)	Absolute eosinopnil count (Per Cmm)	IgE IU/ml
1.	8yrs/F	3 yrs	-	+	9800	588	2760
2.	13yrs/M	4 yrs	-	+	7800	234	2580
3.	9yrs/M	3 yrs	-	+	7700	308	2680
4.	10yrs/M	9 yrs	-	+	9100	728	2850
5.	10yrs/M	8 yrs	-	+	7800	312	2890
6.	10yrs/M	2 yrs	-	+	8400	336	3860
7.	5yrs/M	2 yrs	-	+	6100	156	2870
8.	4 yrs/M	1½yrs	-	+	7900	474	2550

TABLE - XIII : Forced expiratory volume at the time of asthmatic attack and during treatment.

	Case No.	Age yrs	Forced expiratory volume (lit/Mits) At the time of attack lit/mit	visit after attack Ist	During treatment IInd	IIIrd	IVth	Vth
STUDY GROUP	1.	10	100	140	150	180	210	220
	2.	8	70	110	135	150	180	-
	3.	13	140	250	280	300	320	-
	4.	9	115	160	185	200	220	240
	5.	10	70	115	200	220	-	-
	6.	10	110	150	170	210	210	-
	7.	11	140	180	200	220	250	-
	8.	5	40	100	130	140	-	-
	9.	8	120	140	170	160	-	-
	10.	12	160	180	220	280	300	-
	11.	6	110	140	180	-	-	-
	12.	8	85	120	165	-	-	-
	13.	7	120	160	160	190	200	-
	14.	10	110	170	220	230	-	-
	15.	4	80	130	120	130	-	-
	16.	7	110	140	180	210	220	-
CONTROL GROUP	1.	10	260					
	2.	5	230					
	3.	9	250					
	4.	9	240					
	5.	13	350					

12. Peak flow at the time of asthmatic attack and during the treatment :

Table XIII show peak flow had markedly decreased in all the patients at the time of attack. During treatment forced expiratory volume increased on each visit and in each case.

DISCUSSION

DISCUSSION

The present study was conducted in Allergy Clinic, Immunology and Biochemistry laboratory, department of Paediatrics, M.L.B. Medical College & Hospital, Jhansi, to assess the clinical and immunological status viz., absolute eosinophil count, serum complements C3 and C4, serum IgE and spirometry in children suffering from bronchial asthma.

A sample of 21 children was taken which included 16 bronchial asthma cases and 5 healthy control cases. Five healthy cases that constituted the control group had no present or past history of allergy, bronchial asthma or family history of allergy.

Diagnosis was based on detailed history, clinical examination and relevant investigation. From parents or other attendants detailed history was obtained in a chronologic order, regarding the present illness. Emphasis was given to age of onset of first attack, frequency per year, duration of disease, any precipitating factors, family history of allergy (atopy).

Haemoglobin, blood leucocyte count, differential leucocyte count and erythrocyte sedimentation rate were done. Absolute eosinophil count was calculated in all the cases.

Stool test was done by light microscopy for ova and cyst in all cases.

Serum complements C3, C4 and serum IgE level was estimated by single radial immunodeffusion technique in 21 cases which included 5 healthy cases.

Spirometry was done in all the cases.

On the basis of observations depicted in table Ist to XIII various interferences were drawn and are discussed under different headings.

AGE OF ONSET & SEX :

Asthma is a complex disease, probably due to interaction between environmental factors and certain specific agents, in a constitutionally predisposed child. In the present study, age of onset of the disease was between 1 to 6 years in 75% of children (table V). In 1974, Wakhlu and Sharma observed probable age of onset as between 6-12 month in 53.6% children.

Blair (1977) and Skoner, Caliguiri (1988) showed that childhood asthma usually began during the first year of life. Silgel and Rachelefsky (1985) observed that one third of children have the onset before 2 yrs of age and 80% developed symptoms before the age of

5 years. In 1992 Croner and Kjellman observed that 32% children had the onset of bronchial asthma before 1.5 years and 81% before 6 years of age.

The ratio of incidence of this disease is male and female was 3 : 1 in the present study. But William and Nical (1969), Wakhlu and Sharma (1974) observed equal incidence of disease in males and females.

Peskin (1977), reported 2 : 1 ratio of males and females. Ellio (1983) and Wamu (1984) also reported the same sex ratio.

In 1987, Khatua et al, reported that male, female ratio was 1.5 : 1.

Family history at allergy (atopy) :

As shown in table I none of the control cases had positive family history bronchial asthma or any other type of allergy.

In the present study, history of atopy was present in all cases.

Cooke & Veer (1916) showed positive history of atopy in 48% cases of bronchial asthma, as compared to 7% in control cases. In 1920, again, 48% cases of atopy were reported by Adkinson in a study on 400 asthmatic

patients. In 1924, Spain and Cooke observed 58.4% cases with history of atopy, in patients of hay fever and asthma. Bruce (1958) observed that nearly 50% patients of asthma had family history of allergy. High incidence of atopy in cases of bronchial asthma was also reported by Johansson (1967), Spitz (1972) and others.

Rackeman et al (1952) during a large survey concluded that atopy was associated with 82% asthmatic children. On the other hand Pife et al (1981) could not detect atopy in more than 20% of asthmatic children studied. Arsdel et al (1959) observed that offsprings of a single atopic parent had about 50% chances of being atopic and if both parents had atopy, the chances were even greater.

BLOOD COUNTS IN BRONCHIAL ASTHMA :

As shown in table VI none of the patients and control case had haemoglobin below 9 gm%. All the patients and control cases had a total leucocyte count within the normal range (6000 to 11000/cmm). However, mean eosinophil count of 7% was seen in bronchial asthma as compared to control cases (2%).

Acharya (1983) also reported eosinophilia of 10-14% in peripheral smear in his study on childhood asthma. Ghazanshani et al (1976) in 24 patients bronchial asthma found that total eosinophil count was significantly higher in asthmatics (441 ± 384) than in healthy control cases (119 ± 88).

Mean erythrocyte sedimentation rate was also higher in cases of bronchial asthma (27.3 mm Ist hour) as compared to control cases.

Absolute eosinophil count :

Table VII shows eosinophilia (AEC 7250/cmm) in 87.5% (14 cases out of 16 cases) patients of bronchial asthma, as compared to normal absolute eosinophil count (⩽250/cmm) in control cases. In 43.7% cases of bronchial asthma a high degree of eosinophilia (7500/cmm) was observed, in the present study.

Bray and Smith (1931) found that eosinophilia is predominently associated with allergic disorder. In 1967 Lowell found that 28 patients had elevated eosinophil counts (7350/cmm). Further he noticed that eosinophilia was lacking in patients of bronchial asthma as a result of intercurrent infections or as a result of using broncho-dilator drugs.

Wakhlu and Sharma (1974) found eosinophilia in 71% patients of bronchial asthma. Stickney and Heck (1974), Gupta et al (1975), Arshod (1981) observed eosinophilia irrespective of the type of asthma in their study. Agarwal et al (1979) also reported significantly high absolute eosinophil count (917.71 ± 618.9) in cases of bronchial asthma, compared to controls (231.4 ± 105.4). Eosinophilia of varying degree, 10% to 40% was also reported by Acharya (1983).

In present study a few cases of asthma (12.5%) had absolute eosinopenia (AEC ⟨156/Cumm). Lukza and Jone (1982) found eosinopenia (170/cmm) in acute cases of asthma and eosinophilia in stable and chronic asthma.

Complement C3 and C4 level in bronchial asthma :

All cases of bronchial asthma had family history of allergy (atopy) mean C3 level pooled was appreciably lower (0.97 mg/ml) in bronchial asthma cases than that of control cases (1.19mg /ml). The difference was appriciable in male asthmatic (0.95 mg/ml). No difference was found in C4 level between asthmatic and control cases (table-VIII).

Normal C4 level was previously demonstrated by many workers (Godfrey and Hawkesley 1975, Delancy 1976; and Hutchcroft 1978) as in present study. Moreover, most

other studies (Arroyave 1977, Srivastava 1982) C3 level was reported to be low as in the present study (0.97 mg/ml). It has been suggested that low C3 level in acute asthma is the result of consumption of complement components.

Kay et al (1974) observed raised C4 level in cases of allergic asthma and low C4 level in nonallergic asthmatic cases. Godfrey and Howkesley (1975) reported normal C4 level in asthma as observed in the present study. Normal C3, C4 and CH_{50} levels have also been reported in 16 asthma patients with aspirin-idiosyncracy (Delaney et al 1976). In contrast, Weemaes et al (1977) reported significantly depressed C4 and C3 proactivator level in children suffering from asthma as compared to healthy controls. Steven et al (1979), however, showed only insignificant decrease in C3 level and Baur et al (1980) demonstrated high complement level during an immediate asthmatic reaction.

Srivastava et al (1982) demonstrated low C3 level in patients with perennial asthma and in those who had asthma of long duration. They suggested that the complement system in these asthmatic was extremely sensitive to allergens. Even the minute concentration of allergens

in their environment could trigger the complement system and herald the onset of disease. In the present study mean serum C3 level was almost the same in patients with perennial asthma, and those who had seasonal asthma. Moreover C3 level was the same, weather asthma was present for more than or less than that.

IgE in normal children :

Control group of this study comprised of 5 children who did not have a family or personal history of allergy. All of them were free from intestinal parasitic infection and had normal eosinophil count. All of them showed IgE level below 920 IU/ml as shown in table XIV .

Table XIV show serum IgE level in normal subject as reported by various researchers, from India and other countries. Das Gupta (1974) reported mean IgE value of 1025 IU/ml with a wide range of 40-8500 IU/ml while Srivastava et al (1982) reported that normal subjected had serum IgE value below 760 IU/ml. In contrast, Khatua et al (1986) who estimated IgE in normal children from 0-12 years reported a range of 0.6 IU/L to 18.5 IU/L.

Mean IgE as shown in table XIV is much higher in Indian than observed in European population. Johansson et al (1967) reported a mean IgE value of 330 mg/ml (range 105-1394 ng/ml) in the sera of swedish blood donors and took a value of 700 ng/ml as the upper limit of normal. Mean IgE value in children was 160 ng/ml in yet another study (Johansson,1968). Juhih et al (1969), however, reported mean value of 240 ng/ml from the same place. Gleich (1970)from Myo clinic reported mean IgE level of 193 ng/ml in normal subjects and 337 ng/ml in blood donors., taking 540 ng/ml as the upper limit of normal.

A study from Japan (Yamamoto et al 1975) reported similar values (300ng/ml). But in the ethiopian children mean serum IgE concentration, 860 ng/ml and 4400 ng/ml in two groups asthma and allergic rhinitis was 6 and 3 times higher than that of normal swedish children (160 ng/ml) as reported by Johansson (1969).

The figures in table XIV indicate that Indians tend to have higher level of IgE than Europeans. High concentration of serum IgE, probably reflects post parasitic infection (Saha 1975).

TABLE - XIV : Serum IgE level in normal subjects

Sl. No.	Year	Worker	Place	Pt.group	No.	Age (yrs)	IgE level mean (range)	Upper limit of normal IgE	Remarks
1.	1967	Johansson	Sweden	Sera of blood donors	61	-	330ng/ml (105-1394)	700ng/ml	Raised in 5% normal subject.
2.	1969	Juhlin	Sweden	-	-	-	248 ng/ml	-	-
3.	1970	Gleich	Minn	Normal subjects blood donors	32	-	193 ng/ml	540 ng/ml	-
4.	1971	Herderson	Minn	-	-	-	⩽540 ng/ml	540 ng/ml	⩽540ng/ml in 95% of non-allergic
5.	1974	Das Gupta	India	-	-	-	522±323ng/ml	-	-
6.	1975	Saha	India	Normal person	35	-	1025±2101IU/ml (40-8500)	1000 IU/ml	8 pts had level 7 700 IU/ml
7.	1975	Yomamoto	Japan	Children	-	-	300 ng/ml	-	-
8.	1977	Loughlin	Minn	-	95	7-60	74 ng/ml (1-2667)	-	-
9.	1982	Srivastava	India	Normal person	40	-	⩽ 960 IU/ml	760 IU/ml	-
10.	1986	Khatua	India	-	-	0-12	0.6 to 18.5 IU/ml	-	-
11.	1993	Present study	India	Children	16	4-13	⩽920 IU/ml	-	-

Saha (1975) on the basis of previous work by various other authors, considered IgE level of 1000 IU/ml to be abnormal for Indian population. Taking 1000 IU/ml as the baseline, non of the control cases in the present study had abnormally high serum IgE value.

IgE in Bronchial asthma :

Serum IgE value in bronchial asthma cases ranged from 920 IU/ml to 3860 IU/ml, in the present study. Eight out of sixteen cases had IgE value more than 920 IU/ml (2550-3860 IU/ml). Thirteen out of sixteen children had seasonal bronchial asthma and an IgE level of (920 to 3860 IU/ml). Three children who had perennial bronchial asthma had IgE level of (2850 to 2890 IU/ml). IgE level in asthma in expected to be higher during the season of attack, in comparison to level before or after that season (Berg et al 1969).

Berg et al (1969) showed raised IgE value in 2 out of 4 cases of bronchial asthma (with seasonal symptom) as compared to control cases. However, the upper limit of normal IgE value observed in the present study (920 IU/ml or 2162 ng/ml) was much higher than that observed by Berg in his asthmatic cases (540 ng/ml). Higher serum IgE

value in bronchial asthma cases have also been reported by several researchers from India and other countries (Table XV).

Saha et al (1975) reported mean IgE value of 3827 IU/ml in bronchial asthma. Table X show that fifty percent cases in the present study had IgE value more than 920 IU/ml.

Srivastava et al (1982) also reported higher serum IgE value (depending on age of onset, duration and periodicity of disease) above the control group. No differences was found with the duration or periodicity of disease. Almost similar result found in present study.

Total serum IgE was also found to be significantly higher in all patient of bronchial asthma, in comparison to control (Khatua et al 1986). The actual value reported by the auther, were much lower (25-580 KU/L) than observed in the present study (⩾ 920 - 3860/ IU ml) and in same other Indian studies (table XV).

Johansson et al (1967) in one of the earliest studies of serum IgE level in bronchial asthma, reported high IgE value in 63% cases of allergic asthma.

Sl. No.	Year	Worker	Place	Potient age	Clinical group	No.	IgE level mean	IgE level Range	Remarks
1.	1967	Johansson	Sweden	-	Total	39	828ng/ml	(40-4033)	
					Allergic asthma	16	1589 ng/ml	(122-4033)	Increased in 63 cases
					Non-allergic asthma	22	275 ng/ml	(40-1510)	In 5% cases
2.	1969	Berg	Sweden	-	Perineal symp.	09	-	-	In 90% cases
					Seasonal symp.	04	-	-	In 50% cases.
3.	1970	Gleich	Minn	-	Treated	32	1378 ng/ml	-	In all cases
					Not treated	30	2633 ng/ml	-	In all cases
4.	1971	Henderson	Minn	-	Allergic	30	-	-	In 75% cases
					Idiopathic	75	-	-	Increase in 21% cases.
5.	1975	Saha	India	(12-60yrs)	Bronchial asthma	69	3827 IU/ml	-	Increase in 91% cases level 3-5 times higher than normal.
6.	1977	Lin	Pitsberg Children		Bronchial asthma	35	-	-	Increase in 65% cases.
7.	1982	Srivastava	India	-	""	32	1755.5 IU/ml	-	Increase in all group.
8.	1986	Khatua	India	children	""	59	25 to 580 IU/ml	-	-
9.	1993	Present	India	Children (4-13yrs)	Seasonal	13	920-3860IU/ml	-	
					Perennial	03	2850-2890IU/ml		Increase in 50% cases.

In general Ig^E values were higher in all cases of allergic asthma; intreated cases than in untreated cases and in perennial asthma than in seasonal asthma, as observed in the present study. Higher Ig^E value in present study was not associated with eosinophilia or history of atopy.

Spirometry in Bronchial asthma :

Table XIII show all sixteen cases of bronchial asthma had decrease Peak expiratory volume (FEV). The FEV is the single best measure for assessing severity of airflow obstruction. In control cases, who had FEV more than 200 Lt/min as compared to asthmatic patient, who had less than 200 Lt/Min.

In cases of bronchial asthma, the FEV/FVC percentage is greatly reduced, some time 20% or less in reference to normal control which is between 68-80% (Guyton 1991).

Whatever, literature available, I had found that Peak expiratory flow decreased in bronchial asthma patients at the time of attack. In present study peak expiratory flow was decreased in all cases of bronchial asthma at the time of attack. During treatment peak expiratory flow increased in all cases.

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SUMMARY & CONCLUSION

SUMMARY AND CONCLUSION

The present work was carried out to study the serum complement C3 and C4 level, serum IgE level, Absolute eosinophil count and lung capacity by spirometry in bronchial asthma.

The study was conducted in the allergic clinic, immunology and biochemistry laboratory, department of Paediatrics, M.L.B. Medical College, Jhansi over a period of 16 months from Nov.,1991 to Feb.,1993.

The present study comprised of 21 children (4 yrs to 13 yrs of age), which included 16 children of bronchial asthma and 5 healthy control cases.

Diagnosis was based on detailed history, clinical examination and relevant investigation. Emphasis was given to frequency of attacks in a year, age of onset of disease, precipitating factors, history of worm infestation and family history of allergy/bronchial asthma.

Haemoglobin, total leucocyte count, differential leucocyte count, erythrocyte sedimentation rate were done in all the cases. Absolute eosinophil count was calculated and stool examination was done for ova/cyst.

Serum complement C3, C4 and IgE were estimated in all the cases by single radial immuno-diffusion technique. Five children who did not have a personal or family history of allergic disorder and were free from intestinal parasitic infection served as control cases. IgE value could be estimated accurately between 920 IU/ ml to 11,000 IU/ml.

The results of present study are summarized as follows :-

Family history of allergy was positive in all the cases of bronchial asthma. Age of onset was between 1 to 6 yrs in 75% cases of bronchial asthma. In the present study, it was observed that bronchial asthma was common in male as compared to female (3:1) children.

Blood counts in Bronchial asthma :

All the patients and healthy control cases had haemoglobin more than 9 gm percent, and total leucocyte count within the normal range. In cases of bronchial asthma, mean eosinophil count was 7% and ESR ranged between 5 to 56 mm in Ist hour with a mean of 27.3 mm in Ist hour.

Absolute eosinophil count :

Eosinophilia (AEC 7250/cmm) was present in 87.5% cases of bronchial asthma. None of the normal control cases had eosinophilia. Higher degree of ecsinophilia (AEC 7500/cmm) was present 43.7% of asthmatic cases. None of the cases had intestinal parasitic infection. It was observed that highest degree of eosinophilia (mean eosinophil count ; 535/ cmm) was present (5 cases) with more than five years duration of bronchial asthma.

Serum complement C3 and C4 level in bronchial asthma :

Mean C3 level (0.97 mg/ml) was appreciably lower, especially in male (0.95 mg/ml) asthmatics children than that observed in the control group (1.19 mg/ml)Ndifference could be found in mean C4 level between asthmatic (0.28 mg/ml) and normal control cases (0.28 mg/ml). No difference was found in the serum levels of complement C3 and C4, according to duration (more than or less than 5 years) or periodicity (seasonal or perennial) of asthma.

IgE in normal and Bronchial asthma children :

IgE level in all the control cases was ⟨920 IU/ml with no history of atopy, intestinal parasitic infection and eosinophilia. Serum IgE level was high (⟩920 IU/ml) in 50% cases of bronchial asthma (8 out of 16 cases). High level ranged from 2550 IU/ml to 3860 IU/ml. All children of bronchial asthma had history of atopy. None of the cases had intestinal parasitic infection. Serum IgE level did not vary significantly with age. All the three cases of perennial bronchial asthma had raised IgE (⟩920 IU/ml). But, among seasonal asthma cases only five out of thirteen children had raised IgE levels. No difference was noted serum IgE level on the basis of duration of asthma. Higher IgE value in the present study was not associated with eosinophilia or history of atopy.

Spirometry :

Peak flow had markedly decreased in all the cases of bronchial asthma at the time of attack. Following treatment Peak flow increased in all the cases.

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APPENDIX

APPENDIX

WORKING PROFORMA

"A CLINICAL AND IMMUNOLOGICAL STUDY OF BRONCHIAL ASTHMA IN CHILDREN"

Place of work : Allergy Clinic, Immunology and Biochemical Laboratory, Department of Paediatrics, M.L.B. Medical College, Jhansi.

Case No. MRD/OPD No. Code: SKIN/PAED

Name : Age/Sex/D.O.B.

Father's name :

Address :

Diagnosis :

Occupation : Father - Mother -

Total family income : Rs. /month

Per capita income : Rs. /month

Geniological History :

Social - Residence

Vegetarian/Non vegetarian/Eggetarian

Method of excreta disposal

Immunization :	Primary	B1	B2	B3
Polio				
D.P.T.				
B.C.G.				
Measles				
Others				

History of Present Illness

Symptoms	Duration
1. Fever	
2. Cough	
3. Breathlessness	
4. Wheezing	
5. Excessive cry	

6. **Irritability**
7. **Abdominal colic**
8. Itching
9. Loose motions with blood
10. Rashes : Dermatitis
: Urticaria

Related to Ingestants : (Fish, shellfish, nuts, peanuts, food additive drugs etc.)

- Yes/No
- Specific name
- Average Time Interval : Days
: Hours

Related to Injectants : (Drugs, transfused blood, therapeutic antisera, insect stings and bites, allergenic extracts etc.)

- Yes/No
- Specific name
- Average Time Interval : Days
: Hours

Related to contactants : (Plant substances, drugs applied to the skin stinging nettle, animal saliva etc.)

- Yes/No
- Specific name
- Average Time Interval : Days
: Hours

Related to Inhalants : (Pollen, dander ? molds etc.)

- Yes/No
- Specific name
- Average Time Interval : Days
: Hours

Causative/Precipitating Factors : Time interval between exposure and symptoms

- Cold
- Solar

- Aquagenic
- Dermagraphism
- Vibratory
- Physical Exercise
- Emotional stimuli

Specific details duration etc.

- Parasitic infection
- Viral infection
- Bacterial infection
- Fungal infection

Details of Present Illness

1. Duration of symptoms per episode
2. Frequency per year
3. Seasonal variation, if any (Note : specify the season)

History of Past Illness

Note : Specify only the duration

- Measles
- Pertusis
- Chronic diarrhoea
- Worm infestation
- Others
- Urticaria
- Eczema
- Asthma
- Rhinitis

Family History : (Details, if any)

- Koch's Yes/No
- Chronic Illness Yes/No
- Similar Illness Yes/No

History of Atopy : (Asthma, urticaria, atopic dermatitis, Rhinitis, history of angioedema, fever)

Physical Examination :

- Heart rate
- Resp.rate
- Temperature
- Hydration
- Anaemia
- Cyanosis
- Clubbing

Lymphadenopathy

- Cervical
- Axillary

Examination of Skin :

Wheel :

- Size
- Distribution
 - . Scalp
 - . Face
 - . Neck
 - . Trunk
 - . Extremities : Upper - Flexor surface
 Extensor surface
 Lower - Flexor surface
 Extensor surface

Dermatitis :

A. Distribution

- . Scalp
- . Face
- . Neck
- . Trunk
- . Extremities : Upper - Flexor surface
 Extensor surface
 Lower - Flexor surface
 Extensor surface

Nature of lesions

(Groups papules, vasicles, oozing, scaling, mention other features, erythma excoriation)

Blood pressure	mmHg	Oedema	Yes/No
Weight	Kg	Height/Length	cm.
Head circumference	cm.		

SYSTEMIC EXAMINATION

Respiratory system

Inspection

Palpation

Percussion

Auscultation

Cardiovascular system

Signs of CHF

JVP

Hepatomegaly

Basal crepts

Abdomen

- Splean
- Liver
- Colon
- Tenderness
- Lymphnode

Central Nervous system

INVESTIGATIONS

Blood : T.L.C. /cu.mm.

D.L.C. p %, L %, E %, M %, B %.

Hb gm%, ESR mm in 1st hour

Absolute eosinophil count

Urine : Albumin

Sugar

Stool : Cva RBC/Pus cells.

Cyst

X-ray Chest Mx test

Report mm

Date/R. No. Date/Number

IMMUNOLOGIC STUDY (Date of bleeding)

1. Complement level :

 C3 level mg%

 C4 level mg%

2. Immunoglobulins levels :

 IgE IU/Ml

Spirometry :

REATMENT
ND DOSE

Name	Number	Date of Birth	Height cm / in

litres/minute: 100 200 300 400 500 600 700

Time	Day	Date
morn'g / noon / even'g		
morn'g / noon / even'g		
morn'g / noon / even'g		
morn'g / noon / even'g		
morn'g / noon / even'g		
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